Using molecular oxygen and Fe-N/C heterogeneous catalysts to achieve Mukaiyama epoxidations via *in situ* produced organic peroxy acids and acylperoxy radicals

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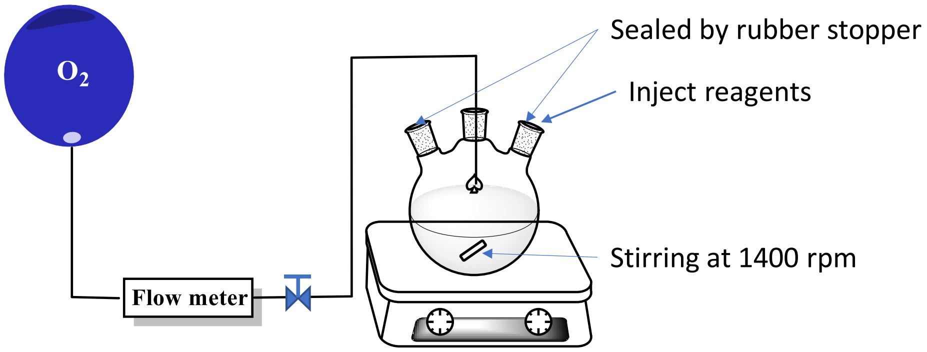
1. Experimental Setup



Supplementary Information Fig.1 The schematic diagram of experimental setup.

The glassware was cleaned in the base bath for at least 4h, rinsed with deionised water (MilliQ 18.2 MΩ cm) and dried in the oven at 110 ºC before use. All the epoxidation reactions and oxidation of aldehyde reactions were done under room temperature (25 ± 2 °C) and the mixture were stirred at 1,400 rpm.

The catalyst (6 mg) and anhydrous acetonitrile (25 mL, 99.9% VWR) were mixed and sonicated for 10 minutes to obtain a homogeneous dispersion. A balloon of oxygen (approx. 2 L, BIP plus-X47S, Air products) was attached. The system was degassed by flushing oxygen for around 5 min and the pressure was balanced before injecting any reagents. Oxygen flow was monitored by a mass flow meter (15 mln/min O2, Bronkhorst Flow Meter). Once the oxygen flow decreased to zero, cyclohexene and aldehyde were added respectively. The reaction was run until the oxygen flow reached zero. All epoxidation reaction followed this procedure, apart from the specific cases noted.

For reduced partial pressure measurement, the solution and system are saturated with air instead of pure oxygen. The balloon is still filled with pure oxygen; so when the oxygen in the reactor is used up, the pure oxygen will flow into the reactor and the partial pressure of oxygen maintain at 20 vol%.

2. Gas chromatography analysis

Syringe filter (0.2 µm PTFE, Merck Millex®) was used to remove the catalyst from mixture and get an aliquot of the sample. Gas chromatography (GC) was used to analyse the components of an aliquot and calculate the yield, conversion and selectivity.

0.5 mL of mesitylene (98%), an internal standard, and 0.8 mL of an aliquot from filtered solution were added into a GC vial (Ghromacol VAGK, Thermo Scientific). 1 µL of sample was taken in the GC (Perkinelmer Clarus 480, FID detector, Astec Chiraldex G-BP: fused silica capillary column 30 m × 0.25 mm × 0.12 µm film thickness, carrier gas: H2 gas (BOC))The flow rate is 12.5 pts/s and the inject temperature is 205 °C. Initial temperature was 50 °C and hold for 10 min. Then, the temperature increases at a speed 10 °C /min to 100 °C and hold for 5 min. Finally, the temperature increases to 180 °C at the same rate and hold for 10 min. All of the calibrated substances are listed in SI Table 1.

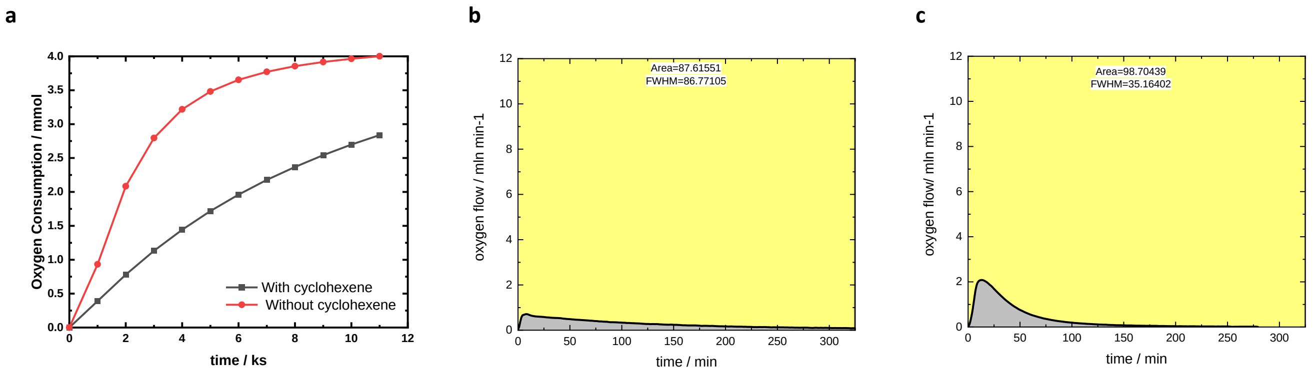
Supplementary Information Table 1. The calibrated retention time of different substance

	Time / min
Cyclohexene oxide	13.0
Isobutyraldehyde	3.0
Butanal	3.5
Hexanal	11.3
Cyclohexene	3.3
2-propanol	3.2
Acetone	2.9
Pivalaldehyde	3.3

$$Conversion\ /\% = \frac{mass\ consumed}{initial\ mass} \times 100$$

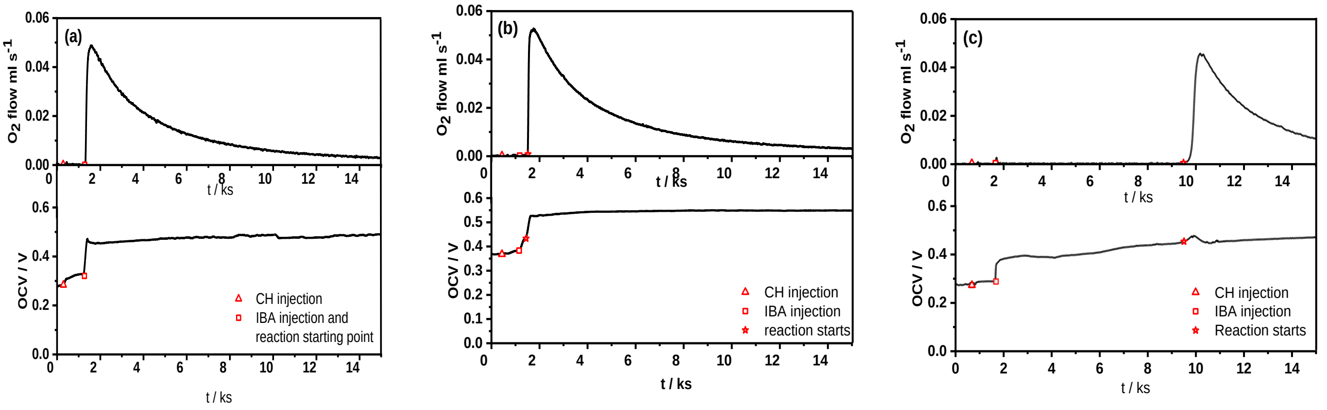
$$Selectivity\ /\% = \frac{m(\ cyclohexene\ consumed)}{m(epoxide\ formed)} \times 100$$

3. Oxygen Consumption without cyclohexene



Supplementary Information Fig.2 Oxygen consumption with and without the addition of cyclohexene. (a) total oxygen consumption at different time (b) the oxygen flow graph with cyclohexene (c) the oxygen flow graph without the addition of cyclohexene. All reactions were taken at 25 ± 2 °C under pure oxygen, 6 mg of Fe-N/C catalyst and 25 cm^{-3} of anhydrous acetonitrile (0.24 $g_{\text{Fe-N/C catalyst}}$ $dm^{-3}_{\text{acetonitrile}}$) were used for (a), (b) and (c).

4. Effect of injecting inhibitor with monitoring the OCP



Supplementary Information Fig. 3 Effect of inhibitor at the early reaction stage (a) Inhibitor free cyclohexene epoxidation (b) inhibitor containing cyclohexene epoxidation (c) 0.01mmol BHT injected at the beginning of inhibitor-free cyclohexene epoxidation

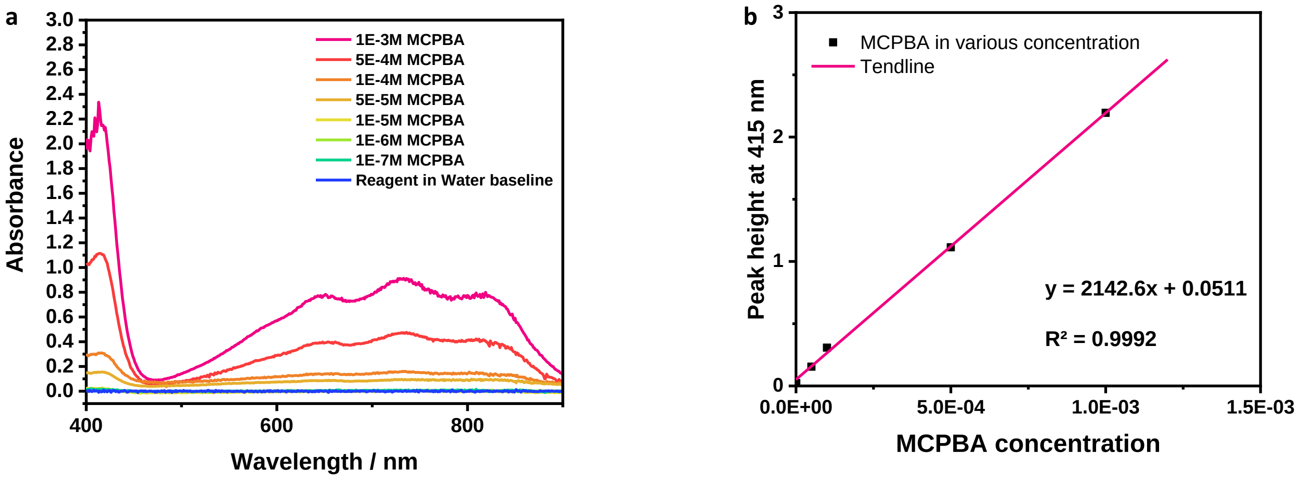
Supplementary Information Table 2. **Inhibitor effect, 25°C, overnight (2.69umol Fe in catalyst)**

	$X_{Cyclohexene}$	$X_{Aldehyde}$	$S_{epoxide}$	Yield	Induction time/h
Inhibitor-free	96.7%	94.5%	82.5%	80.0%	0
2.3 nmol BHT contained CH	98.0%	93.0%	74%	72.5%	0.08
8.7 µmol BHT	94.9%	93.0%	74.3%	70.5%	2

The nature of the radical based mechanism of this reaction was determined by adding 2mg of the radical scavenger butylated hydroxytoluene (BHT) after the reaction starts, a sharp decrease in both reaction rate and OCP measurement was observed.

Varying the amount of BHT added to the reaction has a major effect on the initiation process. Though the inhibitor was only used in a trace amount (Table. SI2), it brought a small drop in the selectivity to epoxide, probably due to the fact the reaction was not allowed to complete for the reactions with the larger amounts of BHT. In contrast to the reactivity difference, the induction time was affected significantly. In an inhibitor-free reaction, no induction time was observed, OCV level increases instantly after cyclohexene injected and raise up to about the final level when isobutyraldehyde is injected. However, in the epoxidation of cyclohexane that contains BHT as the stabiliser, it took several minutes to starts the reaction, and the OCV increases slowly after the aldehyde is injected. Surprisingly, in Figure 7c with only 8.7umol BHT, a two-hour induction period was observed. The OCV measurements recorded the detail of oxide radical being inhibited by trace BHT during initiation. After the isobutyraldehyde was injected, the OCV slowly ramps up till the point that the reaction starts. Comparing the amount of BHT to the iron contents in the catalyst, it is clear that for BHT added less than the iron contents, the induction period is not very long, whereas if BHT is added far more than the Fe sites, it is possible that most active sites will be temporarily blocked. As BHT is more likely to react with the radicals, it can be consumed by generated radicals in hours. This is in agreement with the mechanism propose where the catalyst initiates isobutyraldehyde into radical chain reactions, which also proves the detection sensitivity of this newly developed electrochemistry analysis methods.

5. Calibration of UV-Vis with m-CPBA

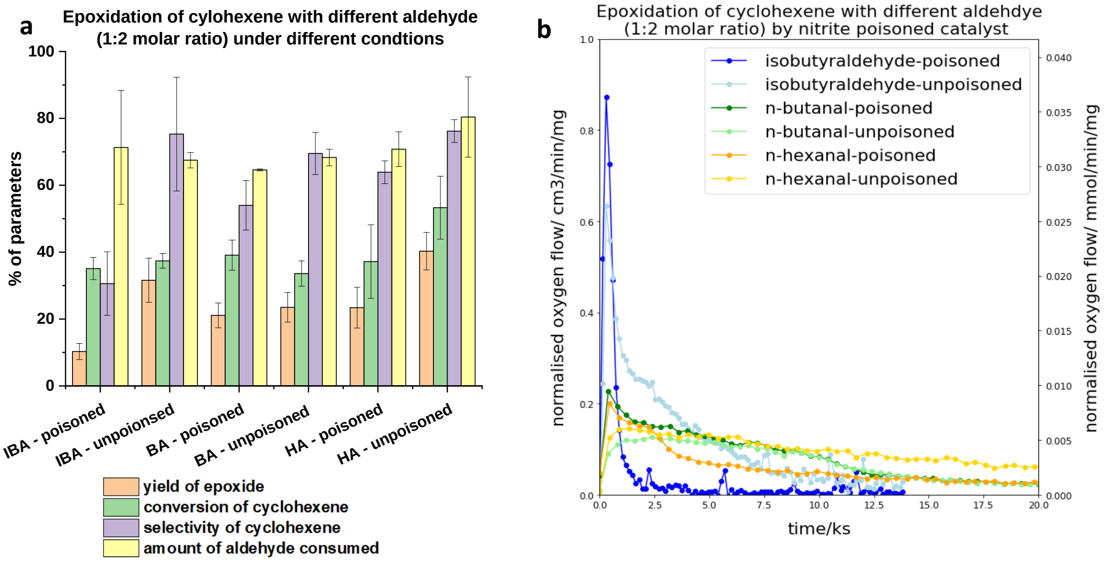


Supplementary Information Fig.4 Calibration of UV-Vis spectrum with different concentration of *m*-CPBA. (a) the UV-Vis spectrum with different concentration of *m*-CPBA in ABTS solution (b) the linear relationship between the peak height at 415 nm and the concentration of *m*-CPBA

For the calibration, the ABTS solution is prepared by 83.3 mg of ABTS. 3.33 mg of KI and 10 mL of acetic acid and the solution was filled up to 500 mL with DI water. *m*-CPBA was dissolved in acetonitrile. 1 mL of premade ABTS solution was mixed with 0.1 mL of m-CPBA with different concentration.

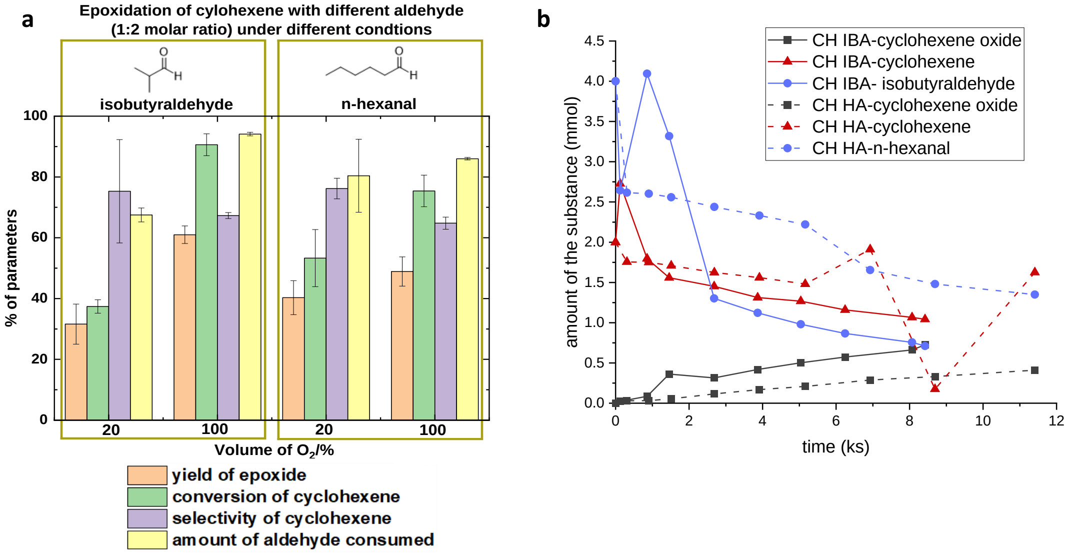
6. Epoxidation reaction with nitrite poisoned Fe-N/C catalyst

The catalyst (40 mg) was grinded manually and then was immersed into 0.125 M sodium nitrite solution for 15 min and the catalyst was washed with water for three times. Finally, the catalyst was dried in the oven at 80 °C under vacuum overnight. The nitrite poisoned catalyst was used for epoxidation and the procedure was same as in Section 1.



Supplementary Information Fig.5 Epoxidation of cyclohexene with different aldehyde and poisoned Fe-N/C catalyst. (a) the yield of epoxide, conversion and selectivity of cyclohexene and the amount of aldehyde consumed with poisoned and unpoisoned catalyst. (b) the oxygen flow diagram of epoxidation with different aldehydes and catalyst. For all reaction, 2 mmol of cyclohexene and 4 mmol of aldehyde were used. 6 mg of catalysts was mixed in 25 mL of dried acetonitrile.

7. Concentration of reactants and product at different reaction time



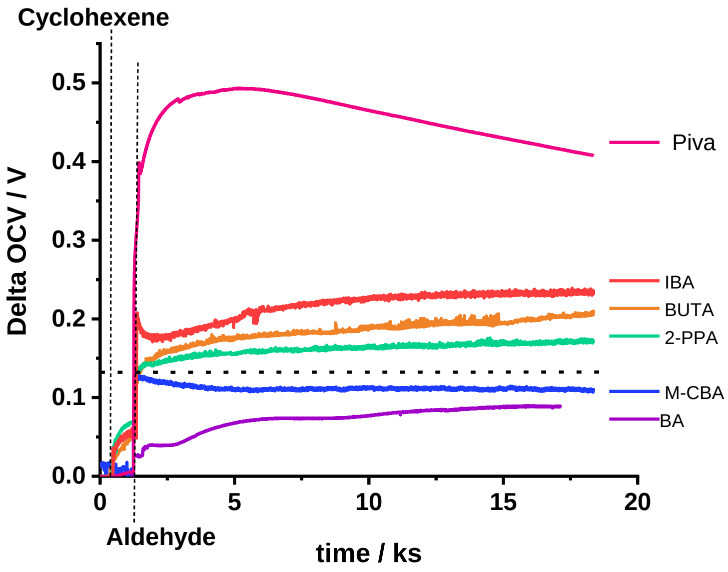
Supplementary Information Fig.6 Cyclohexene epoxidation with isobutyraldehyde and n-hexanal. (a) the yield of epoxide, conversion and selectivity of cyclohexene and the amount of aldehyde consumed under different concentration of oxygen. (b) the amount of substances including reactants and products at different reaction time. [CH: cyclohexene; IBA: isobutyraldehyde; HA: n-hexanal] For all of reactions, 2 mmol of cyclohexene, 4 mmol of aldehyde and 6 mg of Fe-N/C catalyst were mixed in 25 mL of dried acetonitrile.

8. A comparison table about the epoxidation with similar condition

Catalyst	alkene	aldehyde	molar ratio of alkene to aldehyde	homogenous/ heterogenous catalyst	conversion	yield of epoxide
$Fe(acac)_3$[1]	cyclohexene	isobutyraldehyde	1:2.8	homogeneous	78	59
$Ni(OAc)_2\ 4H_2O$[1]	cyclohexene	isobutyraldehyde	1:2.8	homogeneous	82	67
$Co(acac)_2$[1]	cyclohexene	isobutyraldehyde	1:2.8	homogeneous	84	58
$Rh_2(OAc)_4$[2]	1-Phenyl-1-cyclohexene	isovaleraldehyde	1:4	homogeneous	not reported	60
Fe(TPP)Cl[3]	cyclohexene	isobutyraldehyde	3:10	homogeneous	not reported	33
$Fe(cyclam)^{2+}$[3]	cyclohexene	isobutyraldehyde	3:10	homogeneous	not reported	46.7
MIL-53[Cu][4] (30 °C)	cyclohexene	isobutyraldehyde	1:3	Heterogenous	10	9.1
Co@N:C [5] (70 °C 10 bar)	cyclohexene			Heterogenous	80	30
MOF-525-Mn[6]	styrene	isobutyraldehyde	1:5	Heterogenous		83
Fe-N/C(ODAN) (This study)	cyclohexene	isobutyraldehyde	1:2	Heterogenous	92	91

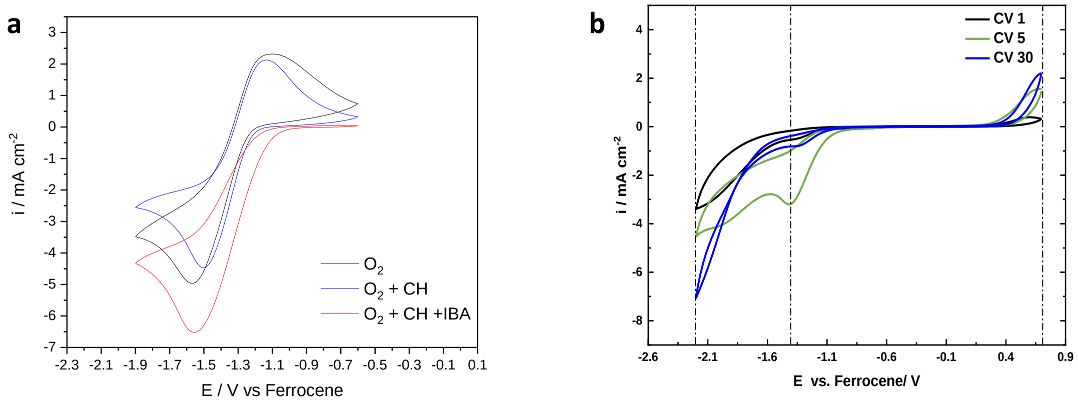
All of reactions are operated under room temperature and pressure unless stated.

9. OCP measurement with different aldehyde



Supplementary Information Fig.7 The OCP measurement versus time of cyclohexene epoxidation with different aldehyde.

10. Cyclic voltammetry of epoxidation



Supplementary Information Fig.8 The cyclic voltammetry of epoxidation. (a) the cyclic voltammetry without Fe-N/C catalyst (b) the long-term scan of cyclic voltammetry of epoxidation with dispersed catalyst with stirring

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